Technical Considerations: the past, present and future of simulation modeling of colorectal cancer

Siddhartha Nambiar, Rachel Townsley, Maria Mayorga
North Carolina State University

Kristen Hassmiller Lich, Stephanie Wheeler
University of North Carolina-Chapel Hill
Background on Colorectal Cancer

- In 2012 only about 65% of individuals were up-to-date with screening
- 27% had never screened
- Improving *screening rates* is a priority
Elements of CRC Simulation Models

- Screening Intervention Model
- Treatment Plan Model
- Patient Health Model
- Cancer Evolution Model
- Population Dynamics Model
- Simulation Models
CRC Simulation Model Paradigms

Discrete Event Simulation Models
- Support for Individual Patient Simulation (IPS).
- Flexibility for patient-patient, patient-environment interaction.

Markov Models
- Enumerate health states a person will experience during the course of the disease.
- The changes in state are described using transition diagrams very similar to flow charts.

Stochastic Microsimulation Models
- “Stochastic" - Models simulate sequences of events by drawing from distributions of probabilities or durations.
- “Microsimulation" - persons are moved through the model one at a time.
CRC Simulation Model- Development History

Simulation Models
- Markov Models
  - Harvard Model
  - UCSF Model
  - Michigan Model
- Stochastic Microsimulation Models
  - Microsimulation Screening Analysis (MISCAN)
  - RTI Model
- CRC Simulated Population Model for Incidence and Natural History (CRC-SPIN)

CISNET Models
- Simulation CRC (SimCRC)
- NC CRC Model
- V-NC Model

Discrete Event Simulation Models
- Vanderbilt Model
Sample Markov Model Structure

- **UCSF (University of California, San Francisco) Model** - a cohort based Markov model from age 50 until death.
- Monte Carlo simulation that runs through the model 3500 times to determine approximate values for the percent of people in each state at a given time.
- Has a small probability for cancer to develop without developing from an adenoma.
V-NC Model

• Primary Simulation Objects
  – Employs an **OOS** (Object Oriented System), driven by a model-independent database.

  – Allows for convenient modeling of causal and treatment pathways.

  – The primary object in the CRC simulation is the **person**.

  – The replication will be terminated when the person dies or when statistics collection ends.
MiCrosimulation SCreening ANalysis (MISCAN)

- MISCAN—Colon is a micro-simulation program, generating individual life histories.
- Uses the Monte Carlo method to simulate all events in the program.
- Possible events are birth and death of a person, adenoma incidence and transitions from one state of disease to another.
North Carolina Colorectal Cancer (NC-CRC) model

Outline-
• Designed to support decision making regarding population screening for colorectal cancer within the state of North Carolina.
• Simulates cancer incidence and mortality by stage, age and calendar year.
• The model can be used to test the effects of various interventions on life-years and costs by increasing an individual’s probability of being screened for CRC.

History-
• Based significantly on the MISCAN-COLON model (Loeve et al. 1999) and the work of Subramanian and colleagues. (2005)
Expansion on other simulation models

– **Applying statistical models** from administrative claims data to predict the preferred screening modality of individuals and compliance with screening.

– **Calibrating natural history parameters** so that the incidence, age and stage of CRC diagnosis closely match registry data specific to the state of NC.

– **Models insurance** and allows status to change over time.

– Incorporating the effects of **population-level interventions** to increase compliance with CRC screening recommendations.
Model Structure

- **Input**
  - Demography: Synthetic population of NC
  - Natural History: Development and incidence of CRC
  - Screening and Testing: Screening compliance and preferred modality

- **Model**
  - Micro-simulation: implemented using AnyLogic®

- **Output**
  - CRC screening: Up to date by age and race
  - CRC cases and deaths: By age, race and stage of diagnosis
  - Costs: Screening for CRC and treatment for CRC

- **Summary Results**
  - Life-years up-to-date, life-years, costs, life-years/cost
Elements of Models

Demography
- Census data
  2005-2010 American Community Survey/Public Use Microdata Sample
  Project from sample to population
- Synthetic population
  Realistic population of all individuals who will be eligible for CRC screening over the 10-year policy window
  Population input file

Natural History
- RTI Model
  Natural history of adenomas and cancer
- Cancer Registry
  Population-based data on incident CRC cases (counts, patient demographics, stage at diagnosis)
  Calibration of CRC natural history parameters
  Parameter estimates
  Predicted probabilities

Screening and Testing
- Claims data
  Medicare, Medicaid, Blue Cross Blue Shield and linked community data such as the Area Resource File
- Literature Review
  Evidence on interventions to increase CRC screening, existing CRC simulation models, and cost studies
  Intervention scenarios
  Approaches for improving population-level screening compliance
  Structural assumptions and parameter values used to simulate each intervention and scenario
  Statistical models
  Logistic regression models predicting individuals’ preferred screening modality and likelihood of compliance

NC-CRC Simulation Model
Geo-spatially explicit, population-based, individual-level discrete-event simulation model of the natural history of CRC progression and screening behaviors
Parameters - Output

NC-CRC Simulation Model
Geo-spatially explicit, population-based, individual-level discrete-event simulation model of the natural history of CRC progression and screening behaviors

- % of the population up-to-date with CRC testing
- Relative impact of alternate intervention approaches on % up-to-date with CRC testing (overall, and by subgroup)
- Cost-effectiveness (efficiency) of alternate intervention approaches
- Disparities in % up-to-date with CRC testing (by sex, race, insurance, and geography)
- Estimated maximum impact of aggressive (i.e., all) intervention on % up-to-date with CRC testing
Object Based Model Structure

Model Structure

- Collection of Person objects.
- Computes event probabilities and population rates.
- Reads input population data.
- Checks if people are due for routine tests.

- Defines parameters for each person.
- Defines how health of a person progresses.
- Defines screening procedure.
- Creates events for each person.

- Collection of tests.
- Defines number of tests, and what tests are offered.

Legend:
- Java Objects: Building blocks of the model.
  Includes variables, parameters, functions, timers and statecharts.
- Statecharts: Part of some objects.
  Define states and when transitions between states are made.
Limitations and Challenges

- Model is highly data intensive.
- Meant to inform population guidelines and is based on general population trends.
- Model can end up requiring extensive computational resources.
Future of CRC Simulation Models

- Optimization algorithms to generate candidate follow-up strategies for specific patient subgroups.

Questions/Discussions/Comments?
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Additional Slides
Assumptions (MISCAN)

- Demography Assumptions
  - The life table differs per birth cohort.
  - Death from colorectal cancer and death from other causes are considered independent from each other.

- Natural History Assumptions
  - Focus on the initiation, progression and response to treatment of colorectal cancer in the model.

- Screening Assumptions
  - Focus on all aspects of screening, including compliance and operational characteristics of the screening process.
Statistical Model Description

\[ \text{logit}(\pi_{ij}) = Y_{ij} = \beta_{0j} + \sum_k \beta_k X_{ik} + \sum_l \beta_l X_{jk} + \epsilon_{ij} \]

\[ \pi_{ij} = \frac{e^{Y_{ij}}}{1 + e^{Y_{ij}}} \]

- \( \pi_{ij} \) - Probability of binary outcome (CRC Screening vs No Screen or Colonoscopy vs FOBT) for person i at county j
- \( \beta_{0j} \) - County level intercept
- \( X_{ik} \) - Person level attributes (race, gender, etc)
- \( X_{jk} \) - County level attributes (distance to endoscopy facility)
Age Cohorts Included In Model

- Age;
- Sex;
- Race (white, black, Hispanic, other);
- Smoking status (current, former, never);
- Household income (<$25,000, $25,000-$50,000, ≥$50,000);
- Insurance status (none, private, Medicare, Medicaid, dual Medicare and Medicaid);
- Education (not complete college, completed college);
- Residential location (zip code).
- State health insurance program participation (SHEP, not a participant, participant)
- Marital status for privately insured individuals (married, unmarried, unknown)
Process flow of lesion progression
Compliance process flow

Testing process flow